Coverage of Drugs and Biologicals for Label and Off-Label Uses

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Approved By: UnitedHealthcare Medicare Reimbursement Policy Committee
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IMPORTANT NOTE ABOUT THIS REIMBURSEMENT POLICY

This policy is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

You are responsible for submission of accurate claims. This reimbursement policy is intended to ensure that you are reimbursed based on the code or codes that correctly describe the health care services provided. UnitedHealthcare reimbursement policies use Current Procedural Terminology (CPT®*), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT or other sources are for definitional purposes only and do not imply any right to reimbursement.

This reimbursement policy applies to all health care services billed on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450). Coding methodology, industry-standard reimbursement logic, regulatory requirements, benefits design and other factors are considered in developing reimbursement policy. This information is intended to serve only as a general resource regarding UnitedHealthcare’s reimbursement policy for the services described and is not intended to address every aspect of a reimbursement situation. Accordingly, UnitedHealthcare may use reasonable discretion in interpreting and applying this policy to health care services provided in a particular case. Further, the policy does not address all issues related to reimbursement for health care services provided to UnitedHealthcare enrollees. Other factors affecting reimbursement may supplement, modify or, in some cases, supersede this policy. These factors may include, but are not limited to: legislative mandates, the physician or other provider contracts, and/or the enrollee’s benefit coverage documents. Finally, this policy may not be implemented exactly the same way on the different electronic claims processing systems used by UnitedHealthcare due to programming or other constraints; however, UnitedHealthcare strives to minimize these variations.

UnitedHealthcare may modify this reimbursement policy at any time by publishing a new version of the policy on this Website. However, the information presented in this policy is accurate and current as of the date of publication.

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Reimbursement Policy

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Application

This reimbursement policy applies to services reported using the Health Insurance Claim Form CMS-1500 or its electronic equivalent or its successor form, and services reported using facility claim form CMS-1450 or its electronic equivalent or its successor form. This policy applies to all products, all network and non-network physicians, and other health care professionals.

The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing UnitedHealthcare. It is not enough to link the procedure code to a correct, payable ICD-9-CM diagnosis code. The diagnosis must be present for the procedure to be paid. Compliance with the provisions in this policy is subject to monitoring by pre-payment review and/or post-payment data analysis and subsequent medical review. The effective date of changes/additions/deletions to this policy is the committee meeting date unless otherwise indicated. CPT codes and descriptions are copyright 2010 American Medical Association (or such other date of publication of CPT). All rights reserved. CPT is a registered trademark of the American Medical Association. Applicable FARS/DFARS restrictions apply to Government use. Fee schedules, relative value units, conversion factors, and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Current Dental Terminology (CDT), including procedure codes, nomenclature, descriptors, and other data contained therein, is copyright by the American Dental Association, 2002, 2004. All rights reserved. CDT is a registered trademark of the American Dental Association. Applicable FARS/DFARS apply.

Summary

Overview

Drugs and biologicals must be determined to meet the statutory definition. Under the statute §1861(t)(1), payment may be made for a drug or biological only where it is included, or approved for inclusion, in the latest official edition of the United States Pharmacopoeia National Formulary (USP-NF), the United States Pharmacopoeia-Drug Information (USD-DI), or the American Dental Association (AOA) Guide to Dental Therapeutics, except for those drugs and biologicals unfavorably evaluated in the ADA Guide to Dental Therapeutics. The inclusion of an item in the USP DI does not necessarily mean that the item is a drug or biological. The USP DI is a database of drug information developed by the U.S. Pharmacopoeia but maintained by Micromedex, which contains medically accepted uses for generic and brand name drug products. Inclusion in such reference (or approval by a hospital committee) is a necessary condition for a product to be considered a drug or biological under the Medicare program, however, it is not enough. Rather, the product must also meet all other program requirements to be determined to be a drug or biological. Combination drugs are also included in the definition of drugs if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the above drug compendia.

Drugs and biologicals are considered approved for inclusion in a compendium if approved under the established procedure by the professional organization responsible for revision of the compendium. An off-label/unlabeled use of a drug is defined as a use for a non-FDA approved indication, that is, one that is not listed on the drug’s official label/prescribing information. An indication is defined as a diagnosis, illness, injury, syndrome, condition, or other clinical parameter for which a drug may be given. Off-label use is further defined as giving the drug in a way that deviates significantly from the labeled prescribing information for a particular indication. This includes but is not necessarily limited to, dosage, route of administration, duration and frequency of administration, and population to whom the drug would be administered. Drugs used for indications other than those in the approved labeling may be covered under Medicare if it is determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literatures and/or accepted standards of medical practice. Determinations as to whether medication is reasonable and necessary for an individual patient are made on appeal on the same basis as all other such determinations (i.e., with support from the peer-reviewed literature, with the advice of medical consultants, with reference to accepted standards of medical practice, and in consideration of the medical circumstance of the individual case).
Reimbursement Guidelines

Use of the drug or biological must be safe and effective and otherwise reasonable and necessary. (See the Medicare Benefit Policy Manual, Chapter 16, “General Exclusions from Coverage,” §20.) Drugs or biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this requirement when used for indications specified on the labeling. Therefore, the program may pay for the use of an FDA approved drug or biological, if:

- It was injected on or after the date of the FDA’s approval;
- It is reasonable and necessary for the individual patient; and
- All other applicable coverage requirements are met.

An unlabeled use of a drug is a use that is not included as an indication on the drug's label as approved by the FDA. FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the contractor determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. The following guidelines identify three categories in which medications would not be reasonable and necessary according to accepted standards of medical practice.

- Not for Particular Illness – Medications given for a purpose other than the treatment of a particular condition, illness, or injury are not covered (except for certain immunizations).
- Injection Method Not Indicated – Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration.
- Excessive Medications – Medications administered for treatment of a disease which exceed the frequency or duration of injections indicated by accepted standards of medical practice are not covered.

If a medication is determined not to be reasonable and necessary for diagnosis or treatment of an illness or injury according to these guidelines, the entire charge will be excluded (i.e., for both the drug and its administration). Also excluded from payment is any charge for other services (such as office visits) which are primarily for the purpose of administering a non-covered injection (i.e., an injection that is not reasonable and necessary for the diagnosis or treatment of an illness or injury).

Effective January 1, 1994, off-label, medically accepted indications of Food and Drug Administration-(FDA) approved drugs and biologicals used in an anti-cancer chemotherapeutic regimen are identified under the indications described below. A regimen is a combination of anti-cancer agents clinically recognized for the treatment of a specific type of cancer. Off-label, medically accepted indications are supported in either one or more of the compendia or in peer-reviewed medical literature. The contractor may maintain its own subscriptions to the listed compendia or peer-reviewed publications to determine the medically accepted indication of drugs or biologicals used off-label in an anti-cancer chemotherapeutic regimen. Compendia documentation or peer-reviewed literature supporting off-label use by the treating physician may also be requested of the physician by the contractor.

Coverage Indications

A medically accepted indication, which is covered by National Government Services is one of the following:

1. An FDA approved, labeled indication or a use supported in the American Hospital Formulary Service Drug Information (AHFS-DI), NCCN Drugs and Biologics Compendium, Thomson Micromedex DrugDex® and Clinical Pharmacology as the acceptable compendia based on CMS' Change Request 6191 (Compendia as Authoritative Sources for Use in the Determination of a "Medically Accepted Indication" of Drugs and Biologicals Used Off-Label in an Anti-Cancer Chemotherapeutic Regimen); or

2. Articles or Local Coverage Determinations (LCDs) published by National Government Services.

The compendia listed above will be accepted at the following levels:

- American Hospital Formulary Service-Drug Information (AHFS-DI) – indication is supportive
- NCCN Drugs and Biologics Compendium - indication is a Category 1 or 2A
- Thomson Micromedex DrugDex® – indication is Class I, Class IIa, or Class IIb or
- Clinical Pharmacology – indication is supportive
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When new off-label uses for drugs are published in the above compendia at the accepted level of recommendation, the effective date for National Government Services coverage of those off-label uses is the date of publication of our revised coverage article, not the date of inclusion in the compendia.

**Coverage Limitations**

If a use is identified as not indicated by CMS or the FDA, or if a use is specifically identified as not indicated in the American Hospital Formulary Services (AHFS), Clinical Pharmacology, NCCN Drugs and Biologics Compendium and/or the Thomson Micromedex DrugDex® compendium, the off-label use is not supported and the drug will not be covered.

Regardless of the evidence supporting coverage for a particular off-label use, payment may only be made if the use is reasonable and necessary for the treatment of illness or injury of the specific patient receiving the drug.

Services related to non-covered services or drugs are also not covered (e.g., administration services).

**References Included (but not limited to):**

**CMS LCD(s)**
Numerous LCDs

**CMS Article(s)**
Numerous Articles

**CMS Benefit Policy Manual**
Chapter 9; § 40.1.6 Medical Appliances and Supplies
Chapter 15; § 50 Drugs and Biologicals
Chapter 16; § 20 Services Not Reasonable and Necessary

**CMS Claims Processing Manual**
Chapter 17 Drugs and Biologicals

**CMS Transmittals**
Transmittal 96, Change Request 6191, Dated 10/24/2008 (Compendia as Authoritative Sources for Use in the Determination of a "Medically Accepted Indication" of Drugs and Biologicals Used Off-Label in an Anti-Cancer Chemotherapeutic Regimen)
Transmittal 758, Change Request 7095, Dated 08/20/2010 (Discarded Drugs and Biological Policy at Contractor Discretion)
Transmittal 1962, Change Request 6711, Dated 04/30/2010 (Discarded Drugs and Biologicals Updates)

**UnitedHealthcare Medicare Advantage Coverage Summaries**
Age Related Macular Degeneration (AMD) Therapy: (Macugen ®, Lucentis ®, Avastin®, EYLEA®)
Blood, Blood Products and Related Procedures and Drugs
Chemotherapy, and Associated Drugs and Treatments
Medications/Drugs (Outpatient/Part B)

**UnitedHealthcare Reimbursement Policies**
Anti-Cancer Chemotherapy for Colorectal Cancer (NCD 110.17)
Aprepitant for Chemotherapy-Induced Emesis (NCD 110.18)
Autologous Cellular Immunotherapy Treatment (NCD 110.22)
Avastin (Bevacizumab)
Camptosar (Irinotecan)
Discarded Drugs and Biologicals
Dimethyl Sulfoxide (DMSO) (NCD 230.12)
Eloxatin (Oxaliplatin)
Erbitux (Cetuximab)
Erythropoietin Stimulating Agent (ESA)
## Coverage of Drugs and Biologicals for Label and Off-Label Uses

- Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (NCD 110.21)
- Eylea (Aflibercept)
- Halaven (Eribulin Mesylate)
- Intravenous Immune Globulin (IVIg)
- Intravenous Immune Globulin for the Treatment of Mucocutaneous Blistering Diseases (250.3)
- Jevtana (Cabazitaxel)
- Laetrile and Related Substances (NCD 30.7)
- L-Dopa (NCD 160.17)
- Lucentis (Ranibizumab)
- Lymphocyte Immune Globulin, Anti-Thymocyte Globulin (Equine) (NCD 260.7)
- Macugen (Pegaptanib)
- Medically Unlikely Edits (MUE)
- Photosensitive Drugs (NCD 80.3)
- Positive Inotropic Agents
- Self Administered Drug(s)
- Vaccination (Immunization)
- Verteporfin (NCD 80.3.1)
- Vitamin B12 Injections to Strengthen Tendons, Ligaments, etc., of the Foot (NCD 150.6)
- Xgeva, Prolia (Denosumab)
- Zoledronic Acid (Zometa® & Reclast®)

### MLN Matters

Article MM6191, Compendia as Authoritative Sources for Use in the Determination of a "Medically Accepted Indication" of Drugs and Biologicals Used Off-Label in an Anti-Cancer Chemotherapeutic Regimen

Article MM7095, Discarded Drugs and Biologicals Policy at Contractor Discretion

Article MM6711, Discarded Drugs and Biologicals Updates

### Others

NCCN Drugs & Biologics Compendium, National Comprehensive Cancer Network Website

Program Integrity Manual § 13.5.1 Reasonable and Necessary Provisions in LCDs, CMS Website

Thomson Micromedex DrugDex® Compendium, Micromedix Website

Social Security Act (Title XVIII) Standard References, Sections:

- 1862(a)(1)(A) Medically Reasonable & Necessary
- 1862(a)(1)(D) Investigational or Experimental
- 1833(e) Incomplete Claim
- 1861(t) (1) Drugs and Biologicals

### History

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<tr>
<td>10/08/2014</td>
<td>Annual review, no changes</td>
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<td>10/23/2013</td>
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